AMENDMENT TO THE CLAIMS

A listing of the claims presented in this patent application appears below. This listing replaces all prior versions and listing of claims in this patent application.

Claim 1 (currently amended): A method of identifying a compound which modulates binding of a ~~natural~~ ligand selected from the group consisting of ~~to the insulin receptor (IR), IGF-1 receptor (IGF-1R), or insulin receptor related receptor (IRR)~~ IGF-I, IGF-II and insulin to IGF-1R, or which modulates signal transduction ~~via~~ by binding to ~~IR,~~ IGF-1R ~~or IRR~~, which method comprises:

(A) assessing the stereochemical complementarity between the compound and a molecule, wherein the molecule comprises

(i) amino acids 1 to 462 of IGF-1R, having the atomic coordinates ~~substantially~~ as shown in Figure 1; or

(ii) a subset of said amino acids[[,]] ~~or~~;

~~(iii) amino acids present in the amino acid sequence of IR or IRR[[,]] that form an equivalent three-dimensional structure to that of the molecule as depicted in Figure 1;~~

(B) ~~obtaining a compound that possesses stereochemical complementarity to the molecule; and~~ selecting and obtaining a compound assessed in step (A) which possesses stereochemical complementarity to the molecule;

(C) ~~testing the compound for its ability to (i) modulate binding of a natural ligand to IR, IGF-1R or IRR or (ii) modulate signal transduction via IR, IGF-1R or IRR~~ testing the compound *in vivo* or *in vitro* for its ability to:

(i) modulate binding of a ligand selected from the group consisting of IGF-I, IGF-II and insulin to IGF-1R, or

(ii) modulate signal transduction by binding to IGF-1R; and

(D) selecting a compound tested in step (C) that has the ability to:

(i) modulate binding of a ligand selected from the group consisting of IGF-I, IGF-II and insulin to IGF-1R, or

(ii) modulate signal transduction by binding to IGF-1R.

Claims 2-20 (canceled).

Claim 21 (currently amended): A computer-assisted method for identifying a compound able to bind to ~~IR~~[[,]] IGF-1R ~~or IRR,~~ using a programmed computer including a processor, an input device, and an output device, including the steps of:

(a) inputting into the programmed computer, through the input device, data comprising the atomic coordinates of the IGF-1R molecule as shown in Figure 1, or a subset thereof;

(b) generating, using computer methods, a set of atomic coordinates of a structure that possesses stereochemical complementarity to the atomic coordinates of the IGF-1R molecule as shown in Figure 1, or a subset thereof, thereby generating a criteria data set;

(c) comparing, using the processor, the criteria data set to a computer database of chemical structures;

(d) selecting from the database, using computer methods, chemical structures which are structurally similar to ~~a portion of~~ said criteria data set; and

(e) outputting, to the output device, the selected chemical structures which are similar to ~~a portion of the~~ said criteria data set.

Claim 22 (canceled).

Claim 23 (currently amended): A computer-assisted method according to claim 21, which further includes the step of obtaining a compound with a chemical structure selected in ~~steps (d) and (e)~~ step (d) or outputted in step (e), and testing the compound for the ability to

prevent binding of a ~~natural~~ ligand ~~to IR, IGF-1R or IRR~~ selected from the group consisting of IGF-I, IGF-II and insulin to IGF-1R.

Claim 24 (currently amended): A computer-assisted method according to claim 21, which further includes the step of obtaining a compound with a chemical structure selected in ~~steps (d) and (e)~~ step (d) or outputted in step (e), and testing the compound for the ability to decrease signal transduction ~~via~~ by binding to ~~IR~~[[,]] IGF-1R ~~or IRR~~.

Claim 25 (canceled).

Claim 26 (currently amended): A computer-assisted method according to claim 21, which further includes the step of obtaining a compound with a chemical structure selected in ~~steps (d) and (e)~~ step (d) and outputted in step (e), and testing the compound for the ability to increase signal transduction ~~via~~ by binding to ~~IR~~[[,]] IGF-1R ~~or IRR~~.

Claims 27-30 (canceled).

Claim 31 (currently amended): The method according to claim [[30]] 1, in which the test in step (C) is a high throughput assay.

Claim 32 and 33 (canceled).

Claim 34 (currently amended): The method of claim 1, wherein step (C)(ii) involves testing the compound for the ability to modulate ~~IR~~[[,]] IGF-1R ~~or IRR~~ mediated cell proliferation.

Claim 35 (currently amended): The method of claim 1, wherein the ~~one or more subsets~~ subset of amino acids in step ~~(a)~~ (A) (ii) is defined by amino acids 191-290 of IGF-1R positioned at atomic coordinates ~~substantially~~ as shown in Figure 1.

Claim 36 (canceled).

Claim 37 (currently amended): The method of claim 1, wherein the ~~one or more subsets~~ subset of amino acids in step ~~(a)~~ (A)(ii) is defined by amino acids 223-274 of IGF-1R positioned at atomic coordinates ~~substantially~~ as shown in Figure 1.

Claim 38 (canceled).

Claim 39 (currently amended): The method of claim 1, which further includes the step of modifying the compound selected in step (B) or step (D) such that the compound comprises structural regions able to make contact with amino acids residues at the surface of the molecule as depicted in Figure 2.

Claim 40 (currently amended): The method of claim 1, which further includes the step of modifying the compound selected in step (B) or step (D) such that the compound comprises structural regions able to make contact with amino acids residues in the region of the interface between the L1 domain and the ~~cys~~ Cys-rich domain as depicted in Figure 2.

Claim 41 (currently amended): The method of claim 1, wherein one or more subsets of amino acids in step ~~(a)~~ (A)(ii) are the amino acids that form the β-sheet of the L1 domain of IGF-1R.

Claim 42 (canceled).

Claim 43 (currently amended): The method of claim 1, in which the compound is identified from test compounds in a database.

Claim 44 (currently amended): The method of claim 1, which further includes the step of selecting a compound that increases signal transduction ~~via~~ by binding to ~~IR~~[[,]] IGF-1R ~~or IRR~~.

Claim 45 (currently amended): The method of claim 1, which further includes the step of selecting a compound that decreases signal transduction ~~via~~ by binding to ~~IR~~[[,]] IGF-1R ~~or IRR~~.

Claim 46 (currently amended): The method of claim 1, which further includes the step of selecting a compound that inhibits or prevents the binding of a ~~natural~~ ligand ~~to IR, IGF-1R or IRR~~ selected from the group consisting of IGF-I, IGF-II and insulin to IGF-1R.

Claim 47 (currently amended): A method of identifying a compound that binds to ~~IR~~[[,]] IGF-1R ~~or IRR~~, the method comprising:

(A) assessing the stereochemical complementarity between the compound and a molecule, wherein the molecule comprises:

(i) amino acids 1 to 462 of IGF-1R, having the atomic coordinates ~~substantially~~ as shown in Figure 1; or

(ii) a subset of said amino acids[[,]] ~~or~~;

~~(iii) amino acids present in the amino acid sequence of IR or IRR that form an equivalent three dimensional structure to that of the molecule as depicted in Figure 1;~~

(B) ~~obtaining a compound that possesses stereochemical complementarity to the molecule~~ selecting and obtaining a compound assessed in step (A) which possesses stereochemical complementarity to the molecule; and

(C) selecting a compound that has ~~a~~ an experimentally determined [[K_b]] K_d or K_I of less than 10^{-6} M for ~~IR~~[[,]] IGF-1R ~~or IRR~~.

Claim 48 (currently amended): The method according to claim 47, wherein the ~~K_b~~ K_d is less than 10^{-8} M

Claim 49 (currently amended): The method according to claim 47, wherein the K_I is less than 10^{-8} M